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Ambient Water Quality Criteria for Cyanides

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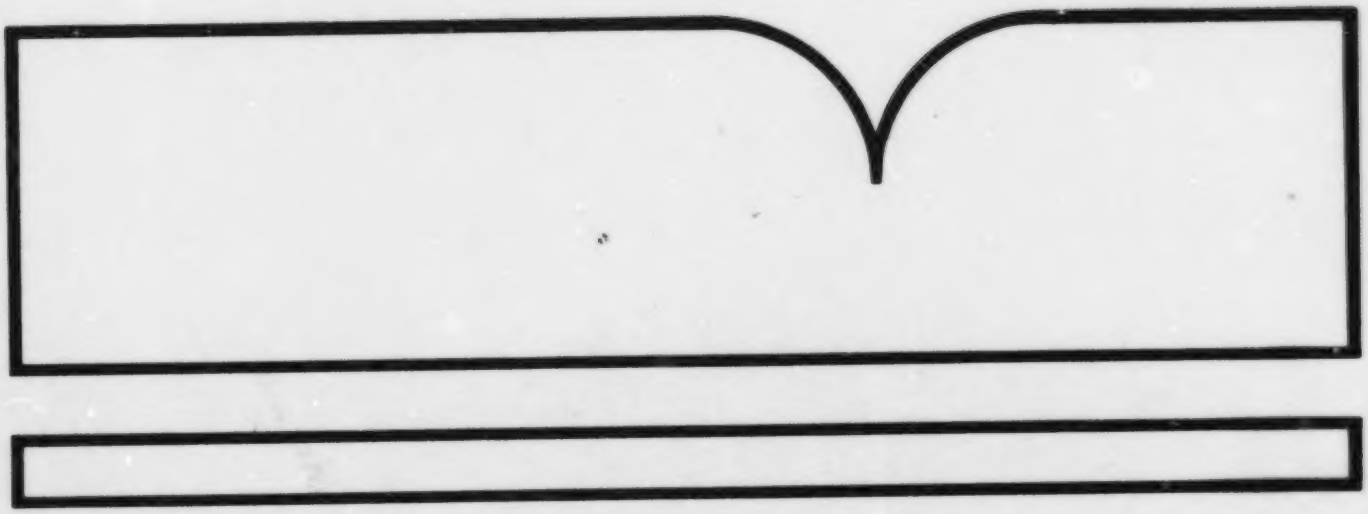

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Ambient Water Quality Criteria for Cyanides

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16. ABSTRACT

Section 304(A) of the Clean Water Act [33 U.S.C. 1314(A)], requires EPA to publish and periodically update water quality criteria. These criteria are to reflect the latest scientific knowledge on the identifiable effects of pollutants on public health and welfare, aquatic life, and recreation. This report presents water quality criteria for Cyanides. It presents concentration criteria for the protection of freshwater and saltwater aquatic life. It presents 'safe' concentrations for humans, and in the case of suspect or proven carcinogens, gives various levels of incremental cancer risk. A Section 304(A) water quality criterion is a qualitative or quantitative estimate of the concentration of a water constituent or pollutant in ambient waters which, when not exceeded, will ensure a water quality sufficient to protect a specified water use. Under the Act a criterion is a scientific entity, based solely on data and scientific judgment. It does not reflect considerations of economic or technological feasibility nor is it a water quality standard and in itself has no regulatory effect.

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AMBIENT WATER QUALITY CRITERIA FOR

CYANIDE

Prepared By
U.S. ENVIRONMENTAL PROTECTION AGENCY

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FOREWORD

Section 304 (a)(1) of the Clean Water Act of 1977 (P.L. 95-217), requires the Administrator of the Environmental Protection Agency to publish criteria for water quality accurately reflecting the latest scientific knowledge on the kind and extent of all identifiable effects on health and welfare which may be expected from the presence of pollutants in any body of water, including ground water. Proposed water quality criteria for the 65 toxic pollutants listed under section 307 (a)(1) of the Clean Water Act were developed and a notice of their availability was published for public comment on March 15, 1979 (44 FR 15926), July 25, 1979 (44 FR 43660), and October 1, 1979 (44 FR 56628). This document is a revision of those proposed criteria based upon a consideration of comments received from other Federal Agencies, State agencies, special interest groups, and individual scientists. The criteria contained in this document replace any previously published EPA criteria for the 65 pollutants. This criterion document is also published in satisifaction of paragraph 11 of the Settlement Agreement in Natural Resources Defense Council, et. al. vs. Train, 8 ERC 2120 (D.D.C. 1976), modified, 12 ERC 1833 (D.D.C. 1979).

The term "water quality criteria" is used in two sections of the Clean Water Act, section 304 (a)(1) and section 303 (c)(2). The term has a different program impact in each section. In section 304, the term represents a non-regulatory, scientific assessment of ecological effects. The criteria presented in this publication are such scientific assessments. Such water quality criteria associated with specific stream uses when adopted as State water quality standards under section 303 become enforceable maximum acceptable levels of a pollutant in ambient waters. The water quality criteria adopted in the State water quality standards could have the same numerical limits as the criteria developed under section 304. However, in many situations States may want to adjust water quality criteria developed under section 304 to reflect local environmental conditions and human exposure patterns before incorporation into water quality standards. It is not until their adoption as part of the State water quality standards that the criteria become regulatory.

Guidelines to assist the States in the modification of criteria presented in this document, in the development of water quality standards, and in other water-related programs of this Agency, are being developed by EPA.

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TABLE OF CONTENTS

	Page
Criteria Summary	
Introduction	A-1
Aquatic Life Toxicology	B-1
Introduction	B-1
Effects	B-3
Acute Toxicity	B-3
Chronic Toxicity	B-4
Plant Effects	B-5
Residues	B-5
Miscellaneous	B-5
Summary	B-6
Criteria	B-7
References	B-28
Mammalian Toxicology and Human Health Effects	C-1
Introduction	C-1
Exposure	C-2
Ingestion from Water	C-4
Ingestion from Food	C-5
Inhalation	C-7
Dermal	C-8
Pharmacokinetics	C-8
Absorption	C-8
Distribution	C-9
Metabolism	C-10
Excretion	C-14
Effects	C-14
Acute, Subacute, and Chronic Toxicity	C-14
Synergism and/or Antagonism	C-20
Teratogenicity, Mutagenicity, and Carcinogenicity	C-22
Criterion Formulation	C-24
Existing Guidelines and Standards	C-24
Special Groups at Risk	C-25
Basis and Derivation of Criteria	C-25
References	C-29

CRITERIA DOCUMENT

CYANIDE

CRITERIA

Aquatic Life

For free cyanide (sum of cyanide present as HCN and CN^-, expressed as CN) the criterion to protect freshwater aquatic life as derived using the Guidelines is 3.5 µg/l as a 24-hour average, and the concentration should not exceed 52 µg/l at any time.

The available data for free cyanide (sum of cyanide present as HCN and CN^-, expressed as CN) indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 30 µg/l and would occur at lower concentrations among species that are more sensitive than those tested. If the acute-chronic ratio for saltwater organisms is similar to that for freshwater organisms, chronic toxicity would occur at concentrations as low as 2.0 µg/l for the tested species and at lower concentrations among species that are more sensitive than those tested.

Human Health

The ambient water quality criterion for cyanide is recommended to be identical to the existing water standard which is 200 µg/l. Analysis of the toxic effects data resulted in a calculated level which is protective of human health against the ingestion of contaminated water and contaminated aquatic organisms. The calculated value is comparable to the present standard. For this reason a selective criterion based on exposure solely from consumption of 6.5 grams of aquatic organisms was not derived.

INTRODUCTION

Cyanides are defined as organic or inorganic compounds which contain the -CN group. Hydrogen cyanide (HCN) is lighter than air and diffuses rapidly. Free HCN is very reactive and occurs only rarely in nature; it is usually prepared commercially from ammonia and methane at elevated temperatures with a platinum catalyst. Hydrogen cyanide is soluble in all proportions in water. It is quite volatile, having a vapor pressure of 100 torr at -178°C; 360 torr at 7°C; 658.7 torr at 21.9°C; and 760 torr at 26.7°C (boiling point) (Towill, et al. 1978). Cyanide ions form complexes with a variety of metals, especially those of the transition series. Ferricyanides and ferrocyanides have a variety of industrial uses but do not release cyanide unless exposed to ultraviolet light. Thus, sunlight can lead to the mobilization of cyanide in waters containing iron cyanides. Cyanogen [$(CN)_2$] is a flammable gas of high toxicity which has a vapor pressure of about 5 atm. at 20°C (Towill, et al. 1978). It reacts slowly with water to produce HCN, cyanic acid, and other compounds. Cyanates contain the -OCN radical. Inorganic cyanates, which are formed industrially by the oxidation of cyanide salts, hydrolyze in water to form ammonia and bicarbonate ion. Alkyl cyanates trimerize readily (when sufficiently concentrated) to form cyanurates. Alkyl isocyanates contain the -NCO radical and are formed from cyanates; they, too, are readily hydrolyzed. Thiocyanates (-SCN radical) are formed from cyanides and sulfur-containing materials and are more stable than cyanates. Solutions of thiocyanates form free hydrogen cyanide in acidic media. Nitriles are organic compounds that have a cyanide group as a substituent. The nitriles are generally much less toxic than the free hydrogen cyanide or the metal cyanides. Cyanohydrins [$R_2C(OH)CN$] are toxic compounds which can decompose with the release of HCN or CN^- under environmental conditions (U.S. EPA, 1979).

REFERENCES

Towill, L.E., et al. 1978. Reviews of the environmental effects of pollutants. V. Cyanide. U.S. EPA. NTIS-PB 289-920. p. 11.

U.S. EPA. 1979. Water-related environmental fate of 129 priority pollutants. Vol. I. EPA 440/4-79-029a.

Aquatic Life Toxicology*

INTRODUCTION

Compounds containing the cyanide group (CN) are used and readily formed in many industrial processes and can be found in a variety of effluents, such as those from the steel, petroleum, plastics, synthetic fibers, metal plating, mining, and chemical industries. Cyanide commonly occurs in water as hydrocyanic acid (HCN), the cyanide ion (CN^-), simple cyanides, metallocyanide complexes, or as simple chain and complex ring organic compounds. "Free cyanide" is defined as the sum of the cyanide present as HCN and as CN^-. The alkali metal salts such as potassium cyanide (KCN) and sodium cyanide (NaCN) are very soluble in aqueous solutions and the resulting cyanide ions readily hydrolyze with water to form HCN. The extent of HCN formation is mainly dependent upon water temperature and pH. At 20^oC and a pH of 8 or below the fraction of free cyanide existing as HCN is at least 0.96.

The cyanide ion (CN^-) can combine with various heavy metal ions to form metallocyanide complex anions, whose stability is highly variable. Zinc and cadmium cyanide complexes, when diluted with water, are known to dissociate rapidly and nearly completely to form HCN. Some of the other metallocyanide anions, such as those formed with copper, nickel, and iron, demonstrate varying degrees of stability. The hexacyanoferrate(II) and -(III) complexes are subject to direct photolysis by natural light. The

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*The reader is referred to the Guidelines for Deriving Water Quality Criteria for the Protection of Aquatic Life and Its Uses in order to better understand the following discussion and recommendation. The following tables contain the appropriate data that were found in the literature, and at the bottom of each table are calculations for deriving various measures of toxicity as described in the Guidelines.

release of cyanide ion by this phenomenon may be important in relatively clear receiving waters.

The toxicity to aquatic organisms of most simple cyanides and metallocyanide complexes is due mostly to the presence of HCN as derived from ionization, dissociation, and photodecomposition of cyanide-containing compounds (Doudoroff, et al. 1966; Smith, et al. 1979), although the cyanide ion (CN^-) is also toxic (Broderius, et al. 1977). In most cases the complex ions themselves have relatively low toxicity. The available literature on the toxicity to fish of cyanides and related compounds was critically reviewed by Doudoroff (1976).

Since both HCN and CN^- are toxic to aquatic life and since the vast majority of free cyanide usually exists as the more toxic HCN, and since almost all existing CN^- can be readily converted to HCN at pH values that commonly exist in surface waters, the cyanide criterion will be stated in terms of free cyanide expressed as CN. Free cyanide is a much more reliable index of toxicity than total cyanide since total cyanide could include nitriles (organic cyanides) and stable metallocyanide complexes. In highly alkaline waters a free cyanide criterion based on the relative toxicity of HCN and the CN^- ion may be appropriate due to the dependence of the form of free cyanide on pH.

All of the cyanide concentrations given herein are free cyanide expressed as CN. Data reported in the original literature as µg of HCN/l were adjusted to free cyanide as CN as follows:

$$(\mu g \text{ of Free Cyanide as CN/l}) = \frac{(\mu g \text{ of HCN/l})\ (1 + 10^{pH-pK_{HCN}})}{} \times \frac{\text{mol. wt. CN}}{\text{mol. wt. HCN}}$$

where $pk_{HCN} = 1.3440 + \frac{2347.2}{T + 273.16}$ (Izatt, et al. 1962)

where T = degrees Celsius.

EFFECTS

Acute Toxicity

The results of 7 acute tests with 6 freshwater invertebrate species are given in Table 1. With three exceptions (Oseid and Smith, 1979; U.S. EPA, 1980a), results are based on static tests with unmeasured concentrations. Most of the species tested were considerably more tolerant than fishes. Daphnia pulex and Gammarus pseudolimnaeus, however, were comparable to fishes in sensitivity. There was greater variability in sensitivity of invertebrate species to free cyanide than was observed for fish species.

The 96-hour LC_{50} values based on acute toxicity tests with 10 fish species are summarized in Table 1. The greatest number of tests were conducted with brook trout, bluegill, and fathead minnows. About 80 percent of the data resulted from studies conducted by Smith, et al. (1978) and Broderius, et al. (1977). All of their tests were conducted using flow-through techniques with the reported HCN levels calculated from analytically measured free cyanide concentrations.

Certain life stages and species of fishes appear to be more sensitive to cyanide than others. Embryos, sac fry, and warmwater species tended to be the most resistant. A review of pertinent data for juvenile fishes indicates that free cyanide concentrations in the range from about 50 to 200 µg/l have eventually proven fatal to most of the more sensitive fish species, with concentrations much above 200 µg/l being rapidly fatal to most fish species. Thus there is a relatively narrow range of species sensitivity for fish. A comparison of acute toxicity results for fishes supports the

hypothesis that the toxicity of simple cyanide solutions is underestimated by static tests, especially when the cyanide concentrations in the test solutions are not measured.

A number of authors have reported an increase in toxicity of cyanide with reduction in dissolved oxygen below the saturation level (Doudoroff, 1976; Smith, et al. 1978). The tolerance of fishes to cyanide solutions that are rapidly lethal has been observed to decrease with a rise of temperature. Long-term lethality tests, however, have demonstrated that juvenile fishes are more susceptible to cyanide with a reduction in temperature (Smith, et al. 1978). No pronounced relationship has been observed between the acute toxicity of cyanide to fishes and alkalinity, hardness, or pH below about 8.3.

Based on Species Mean Acute Values summarized in Table 3, the Freshwater Final Acute Value, derived using the calculation procedures described in the Guidelines, is 52 µg/l.

For saltwater species, acute toxicity data are available for three invertebrate and one fish species and range from 30 to 372 µg/l. These few values suggest that free cyanide is very toxic to saltwater species, which have about the same sensitivity as freshwater organisms.

Chronic Toxicity

The long-term survival and growth of various freshwater fish species was observed to be seriously reduced at free cyanide concentrations of about 20 to 50 µg/l (Kimball, et al. 1978; Koenst, et al. 1977) (Table 5). Results from only a few full and partial life cycle chronic tests with fishes have been reported (Table 2). Based on reduced long-term survival in an early life stage test with bluegills and reduced reproduction by brook trout and fathead minnows in a partial life cycle and life cycle test, the chronic values were 14, 7.9, and 16 µg/l, respectively.

Two freshwater invertebrate life cycle tests (Table 2) were conducted; one with the isopod, Asellus communis, and the other with the scud, Gammarus pseudolimnaeus. The chronic values were 34 and 18 µg/l, respectively.

The Final Acute-Chronic Ratio of 14.8 is the geometric mean of the five acute-chronic ratios (Table 3). The Freshwater Final Acute Value of 52 µg/l divided by the Final Acute-Chronic Ratio of 14.8 results in the Freshwater Final Chronic Value for free cyanide (expressed as CN) of 3.5 µg/l (Table 3).

No chronic data are available for cyanide and any saltwater species.

Plant Effects

Data on the toxicity of free cyanide to one freshwater and two saltwater species of algae are presented in Table 4. Apparently algae are not very sensitive to cyanide when compared with other aquatic organisms, and adverse effects of cyanide on plants are unlikely at concentrations protective of acute effects on most freshwater and saltwater invertebrate and fish species.

Residues

No residue data were found for cyanide.

Miscellaneous

Table 5 contains no data that would alter the selection of 3.5 µg/l as the Final Chronic Value. In fact, there are some pertinent additional studies, on physiological and behavioral responses of fishes to low levels of free cyanide, that are supportive of the calculated chronic value.

Several authors (Neil, 1957; Broderius, 1970; Dixon, 1975; Lesniak, 1977; Leduc, 1978; Oseid and Smith, 1979; Rudy, et al. 1979) reported adverse effects due to cyanide at concentrations as low as 10 µg/l. In another study, Kimball, et al. (1978) reported that no reproduction occurred among adult bluegills when exposed for 289 days to the lowest concentration tested (5.2 µg of HCN/l = 5.4 µg of free cyanide as CN/l). During this

period, however, only a total of 13 spawnings occurred in two controls and no dose-response relationship was observed. Because of reservations regarding the spawning data, the chronic value for bluegills was based on long term fry survival. On the other hand, the most sensitive adverse effect caused by cyanide on both fathead minnows and brook trout was reduced reproduction. The freshwater Final Chronic Value of 3.5 µg/l, based on fish and invertebrate chronic data, appears to be supported by these miscellaneous studies.

Summary

All concentrations herein for free cyanide (sum of cyanide present as HCN and CN^-) are expressed as CN. The data used in deriving the criterion are predominantly from flow-through tests in which toxicant concentrations were measured.

Data on the acute toxicity of free cyanide are available for a wide variety of freshwater organisms that are involved in diverse community functions. Except for the more sensitive invertebrate species, such as Daphnia pulex and Gammarus pseudolimnaeus, invertebrate species are usually more tolerant of cyanide than are freshwater fish species, which have most acute values clustered between 50 to 200 µg/l. A long-term survival and two life cycle tests with fish gave chronic values of 7.9, 14, and 16 µg/l, respectively. Chronic data for the freshwater invertebrate species were more variable, with Gammarus pseudolimnaeus being comparable to fishes in sensitivity and isopods being considerably more tolerant.

The acute toxicity of free cyanide to saltwater organisms is comparable to that observed for freshwater organisms, but no data are available concerning chronic toxicity. For saltwater aquatic life no criterion for free cyanide can be derived using the Guidelines.

Plants are much more resistant to cyanide than animals and thus their well-being is assured if more sensitive aquatic animals are protected.

CRITERIA

For free cyanide (sum of cyanide present as HCN and CN^-, expressed as CN) the criterion to protect freshwater aquatic life as derived using the Guidelines is 3.5 µg/l as a 24-hour average, and the concentration should not exceed 52 µg/l at any time.

The available data for free cyanide (sum of cyanide present as HCN and CN^- expressed as CN) indicate that acute toxicity to saltwater aquatic life occurs at concentrations as low as 30 µg/l and would occur at lower concentrations among species more sensitive than those tested. If the acute-chronic ratio for saltwater organisms is similar to that for freshwater organisms, chronic toxicity would occur at concentrations as low as 2.0 µg/l for the tested species and at lower concentrations among species that are more sensitive than those tested.

Table 1. Acute values for cyanide

Species	Method[a]	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
		FRESHWATER SPECIES		
Snail, *Physa heterostropha*	S, U	432	-	Patrick, et al. 1968
Snail, *Physa heterostropha*	S, U	431	431	Cairns & Scheier, 1958
Cladoceran, *Daphnia pulex*	S, U	83	83	Lee, 1976
Isopod, *Asellus communis*	FT, M	2,326	2,326	Oseid & Smith, 1979
Scud, *Gammarus pseudolimnaeus*	FT, M	167	167	Oseid & Smith, 1979
Midge, *Tanytarsus dissimilis*	S, M	2,240	2,240	U.S. EPA, 1980a
Brook trout (sac fry), *Salvelinus fontinalis*	FT, M	105	-	Smith, et al. 1978
Brook trout (sac fry), *Salvelinus fontinalis*	FT, M	342	-	Smith, et al. 1978
Brook trout (sac fry), *Salvelinus fontinalis*	FT, M	507	-	Smith, et al. 1978
Brook trout (sac fry), *Salvelinus fontinalis*	FT, M	252	-	Smith, et al. 1978
Brook trout (swim-up fry), *Salvelinus fontinalis*	FT, M	84	-	Smith, et al. 1978
Brook trout (swim-up fry), *Salvelinus fontinalis*	FT, M	54.4	-	Smith, et al. 1978
Brook trout (swim-up fry), *Salvelinus fontinalis*	FT, M	86.5	-	Smith, et al. 1978
Brook trout (swim-up fry), *Salvelinus fontinalis*	FT, M	104	-	Smith, et al. 1978

Table 1. (Continued)

Species	Method*	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Brook trout (swim-up fry), Salvelinus fontinalis	FT, M	90.3	-	Smith, et al. 1978
Brook trout (juvenile), Salvelinus fontinalis	FT, M	73.5	-	Smith, et al. 1978
Brook trout (juvenile), Salvelinus fontinalis	FT, M	83	-	Smith, et al. 1978
Brook trout (juvenile), Salvelinus fontinalis	FT, M	75	-	Smith, et al. 1978
Brook trout (juvenile), Salvelinus fontinalis	FT, M	86.4	-	Smith, et al. 1978
Brook trout (juvenile), Salvelinus fontinalis	FT, M	91.9	-	Smith, et al. 1978
Brook trout (juvenile), Salvelinus fontinalis	FT, M	99	-	Smith, et al. 1978
Brook trout (juvenile), Salvelinus fontinalis	FT, M	96.7	-	Smith, et al. 1978
Brook trout (juvenile), Salvelinus fontinalis	FT, M	112	-	Smith, et al. 1978
Brook trout (juvenile), Salvelinus fontinalis	FT, M	52	-	Smith, et al. 1978
Brook trout (juvenile), Salvelinus fontinalis	FT, M	60.2	-	Smith, et al. 1978
Brook trout (juvenile), Salvelinus fontinalis	FT, M	66.8	-	Smith, et al. 1978
Brook trout (juvenile), Salvelinus fontinalis	FT, M	71.4	-	Smith, et al. 1978
Brook trout (juvenile), Salvelinus fontinalis	FT, M	97	-	Smith, et al. 1978

Table 1. (Continued)

Species	Method[a]	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Brook trout (juvenile), Salvelinus fontinalis	FT, M	143	-	Smith, et al. 1978
Brook trout (adult), Salvelinus fontinalis	FT, M	156	103	Cardwell, et al. 1976
Rainbow trout (juvenile), Salmo gairdneri	FT, M	57	57	Smith, et al. 1978
Goldfish (juvenile), Carassius auratus	FT, M	318	318	Cardwell, et al. 1976
Fathead minnow (fry), Pimephales promelas	FT, M	120	-	Smith, et al. 1978
Fathead minnow (fry), Pimephales promelas	FT, M	98.7	-	Smith, et al. 1978
Fathead minnow (fry), Pimephales promelas	FT, M	81.8	-	Smith, et al. 1978
Fathead minnow (fry), Pimephales promelas	FT, M	110	-	Smith, et al. 1978
Fathead minnow (fry), Pimephales promelas	FT, M	116	-	Smith, et al. 1978
Fathead minnow (juvenile), Pimephales promelas	FT, M	119	-	Smith, et al. 1978
Fathead minnow (juvenile), Pimephales promelas	FT, M	126	-	Smith, et al. 1978
Fathead minnow (juvenile), Pimephales promelas	FT, M	81.5	-	Smith, et al. 1978
Fathead minnow (juvenile), Pimephales promelas	FT, M	124	-	Smith, et al. 1978
Fathead minnow (juvenile), Pimephales promelas	FT, M	137	-	Smith, et al. 1978

Table 1. (Continued)

Species	Method[a]	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Fathead minnow (juvenile), Pimephales promelas	FT, M	131	-	Smith, et al. 1978
Fathead minnow (juvenile), Pimephales promelas	FT, M	105	-	Smith, et al. 1978
Fathead minnow (juvenile), Pimephales promelas	FT, M	119	-	Smith, et al. 1978
Fathead minnow (juvenile), Pimephales promelas	FT, M	131	-	Smith, et al. 1978
Fathead minnow (juvenile), Pimephales promelas	FT, M	122	-	Smith, et al. 1978
Fathead minnow (juvenile), Pimephales promelas	FT, M	161	-	Smith, et al. 1978
Fathead minnow (juvenile), Pimephales promelas	FT, M	188	-	Smith, et al. 1978
Fathead minnow (juvenile), Pimephales promelas	FT, M	175	-	Smith, et al. 1978
Fathead minnow (juvenile), Pimephales promelas	FT, M	163	-	Smith, et al. 1978
Fathead minnow (juvenile), Pimephales promelas	FT, M	169	-	Smith, et al. 1978
Fathead minnow (juvenile), Pimephales promelas	S, U	230	-	Doudoroff, 1956
Fathead minnow (juvenile), Pimephales promelas	FT, M	120	-	Broderius, et al. 1977
Fathead minnow (juvenile), Pimephales promelas	FT, M	113	-	Broderius, et al. 1977
Fathead minnow (juvenile), Pimephales promelas	FT, M	128	-	Broderius, et al. 1977

Table 1. (Continued)

Species	Method[a]	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Fathead minnow (juvenile), Pimephales promelas	FT, M	128	-	Broderius, et al. 1977
Fathead minnow, Pimephales promelas	S, M	350	-	Henderson, et al. 1961
Fathead minnow, Pimephales promelas	S, M	230	125	Henderson, et al. 1961
Mosquitofish, Gambusia affinis	S, U	639	639	Wallen, et al. 1957
Guppy (adult), Poecilia reticulata	FT, M	147	147	Anderson & Weber, 1975
Bluegill (fry), Lepomis macrochirus	FT, M	364	-	Smith, et al. 1978
Bluegill (fry), Lepomis macrochirus	FT, M	232	-	Smith, et al. 1978
Bluegill (fry), Lepomis macrochirus	FT, M	279	-	Smith, et al. 1978
Bluegill (fry), Lepomis macrochirus	FT, M	273	-	Smith, et al. 1978
Bluegill (juvenile), Lepomis macrochirus	FT, M	81	-	Smith, et al. 1978
Bluegill (juvenile), Lepomis macrochirus	FT, M	85.7	-	Smith, et al. 1978
Bluegill (juvenile), Lepomis macrochirus	FT, M	74	-	Smith, et al. 1978
Bluegill (juvenile), Lepomis macrochirus	FT, M	100	-	Smith, et al. 1978
Bluegill (juvenile), Lepomis macrochirus	FT, M	107	-	Smith, et al. 1978

Table 1. (Continued)

Species	Method[a]	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Bluegill (juvenile), Lepomis macrochirus	FT, M	99	-	Smith, et al. 1978
Bluegill (juvenile), Lepomis macrochirus	FT, M	113	-	Smith, et al. 1978
Bluegill (juvenile), Lepomis macrochirus	FT, M	121	-	Smith, et al. 1978
Bluegill (juvenile), Lepomis macrochirus	FT, M	126	-	Smith, et al. 1978
Bluegill (juvenile), Lepomis macrochirus	S, U	180	-	Cairns & Scheler, 1958
Bluegill, Lepomis macrochirus	S, U	180	-	Patrick, et al. 1968
Bluegill (juvenile), Lepomis macrochirus	S, M	150	-	Henderson, et al. 1961
Bluegill (juvenile), Lepomis macrochirus	S, M	160	137	Cairns & Scheler, 1963
Largemouth bass (juvenile), Micropterus salmoides	FT, M	102	102	Smith, et al. 1979
Black crappie, Pomoxis nigromaculatus	FT, M	102	102	Smith, et al. 1979
Yellow perch (fry), Perca flavescens	FT, M	288	-	Smith, et al. 1978
Yellow perch (fry), Perca flavescens	FT, M	330	-	Smith, et al. 1978
Yellow perch (juvenile), Perca flavescens	FT, M	88.9	-	Smith, et al. 1978
Yellow perch (juvenile), Perca flavescens	FT, M	93	-	Smith, et al. 1978

Table 1. (Continued)

Species	Method*	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Yellow perch (juvenile), Perca flavescens	FT, M	74.7	-	Smith, et al. 1978
Yellow perch (juvenile), Perca flavescens	FT, M	94.7	-	Smith, et al. 1978
Yellow perch (juvenile), Perca flavescens	FT, M	101	-	Smith, et al. 1978
Yellow perch (juvenile), Perca flavescens	FT, M	107	125	Smith, et al. 1978
		SALTWATER SPECIES		
Copepod, Acartia clausi	S, U	30	30	U.S. EPA, 1980b
Mysid shrimp, Mysidopsis bahia	S, U	93	93	U.S. EPA, 1980b
Mysid shrimp, Mysidopsis bigelowi	S, U	124	124	U.S. EPA, 1980b
Winter flounder, Pseudopleuronectes americana	S, U	372	372	U.S. EPA, 1980b

* S = static, FT = flow-through, U = unmeasured, M = measured

Table 2. Chronic values for cyanide

Species	Test*	Limits (µg/l)	Chronic Value (µg/l)	Reference
		FRESHWATER SPECIES		
Isopod, *Asellus communis*	LC	29-40	34	Oseid & Smith, 1979
Scud, *Gammarus pseudolimnaeus*	LC	16-21	18	Oseid & Smith, 1979
Brook trout, *Salvelinus fontinalis*	LC	5.6-11.0	7.8	Koenst, et al. 1977
Fathead minnow, *Pimephales promelas*	LC	13.3-20.2	16	Lind, et al. 1977
Bluegill, *Lepomis macrochirus*	ELS	9.3-19.8	14	Kimball, et al. 1978

* LC = life cycle or partial life cycle; ELS = early life stage

Acute-Chronic Ratios

Species	Acute Value (µg/l)	Chronic Value (µg/l)	Ratio
Isopod, *Asellus communis*	2,326	34	68
Scud, *Gammarus pseudolimnaeus*	167	18	9.3
Brook trout, *Salvelinus fontinalis*	103	7.8	13
Fathead minnow, *Pimephales promelas*	141	16	8.8

Table 2. (Continued)

Acute-Chronic Ratios

Species	Acute Value (µg/l)	Chronic Value (µg/l)	Ratio
Bluegill, *Lepomis macrochirus*	137	14	9.8

Table 3. Species mean acute values and acute-chronic ratios for cyanide

Rank*	Species	Species Mean Acute Value (µg/l)	Species Mean Acute-Chronic Ratio
	FRESHWATER SPECIES		
15	Isopod, *Asellus communis*	2,326	68
14	Midge, *Tanytarsus dissimilis*	2,240	-
13	Mosquitofish, *Gambusia affinis*	639	-
12	Snail, *Physa heterostropha*	431	-
11	Goldfish, *Carassius auratus*	318	-
10	Scud, *Gammarus pseudolimnaeus*	167	9.3
9	Guppy, *Poecilia reticulata*	147	-
8	Bluegill, *Lepomis macrochirus*	137	9.8
7	Fathead minnow, *Pimephales promelas*	125	8.8
6	Yellow perch, *Perca flavescens*	125	-
5	Brook trout, *Salvelinus fontinalis*	103	13
4	Largemouth bass, *Micropterus salmoides*	102	-
3	Black crappie, *Pomoxis nigromaculatus*	102	-

Table 3. (Continued)

Rank*	Species	Species Mean Acute Value (µg/l)	Species Mean Acute-Chronic Ratio
2	Cladoceran, *Daphnia pulex*	83	-
1	Rainbow trout, *Salmo gairdneri*	57	-
	SALTWATER SPECIES		
4	Winter flounder, *Pseudopleuronectes americana*	372	-
3	Mysid shrimp, *Mysidopsis bigelowi*	124	-
2	Mysid shrimp, *Mysidopsis bahia*	93	-
1	Copepod, *Acartia clausi*	30	-

* Ranked from least sensitive to most sensitive based on species mean acute value.

Freshwater Final Acute Value = 52 µg/l

Final Acute-Chronic Ratio = 14.8

Freshwater Final Chronic Value = (52 µg/l)/14.8 = 3.5 µg/l

Table 4. Plant values for cyanide

Species	Effect	Result (µg/l)	Reference
	FRESHWATER SPECIES		
Blue-green alga, *Microcystis aeruginosa*	90% kill	7,990	Fitzgerald, et al. 1952
	SALTWATER SPECIES		
Green alga, *Prototheca zopfi*	Respiration inhibition	3,000	Webster & Hackett, 1965
Green alga, *Chlorella* sp	Enzyme inhibition	30,000	Nelson & Tolbert, 1970

Table 5. Other data for cyanide

Species	Duration	Effect	Result (µg/l)	Reference
		FRESHWATER SPECIES		
Snail, Goniobasis livescens	48 hrs	LC50	760,000	Cairns, et al. 1976
Snail, Lymnaea emarginata	48 hrs	LC50	3,300	Cairns, et al. 1976
Snail (embryo), Lymnaea spp.	96 hrs	LC50	51,900	Dowden & Bennett, 1965
Snail, Physa integra	48 hrs	LC50	1,350	Cairns, et al. 1976
Scud, Gammarus pseudolimnaeus	98 days	Competition with Asellus affects HCN toxicity	9	Oseid & Smith, 1979
Cladoceran, Daphnia magna	96 hrs	LC50	160	Dowden & Bennett, 1965
Mayfly, Stenonema rubrum	48 hrs	LC50	500	Roback, 1965
Caddisfly, Hydropsyche sp	48 hrs	LC50	2,000	Roback, 1965
Coho salmon, Oncorhynchus kisutch	2 hrs	Swimming speed reduced	10	Broderius, 1970
Chinook salmon (juvenile), Oncorhynchus tshawytscha	64 days	27% reduction in biomass	20	Nagiiski, 1973
Rainbow trout (juvenile), Salmo gairdneri	250 min	Approximate median survival time	200	Dep. Sci. Ind. Res., 1956
Rainbow trout (adult), Salmo gairdneri	2 min	Mean survival time	2,000	Herbert & Merkens, 1952
Rainbow trout (adult), Salmo gairdneri	8 min	Mean survival time	300	Herbert & Merkens, 1952

Table 5. (Continued)

Species	Duration	Effect	Result (µg/l)	Reference
Rainbow trout (adult), Salmo gairdneri	12 min	Mean survival time	250	Herbert & Merkens, 1952
Rainbow trout (adult), Salmo gairdneri	12 min	Mean survival time	200	Herbert & Merkens, 1952
Rainbow trout (adult), Salmo gairdneri	24 min	Mean survival time	180	Herbert & Merkens, 1952
Rainbow trout (adult), Salmo gairdneri	72 min	Mean survival time	160	Herbert & Merkens, 1952
Rainbow trout (adult), Salmo gairdneri	90 min	Mean survival time	140	Herbert & Merkens, 1952
Rainbow trout (adult), Salmo gairdneri	2,525 min	Mean survival time	100	Herbert & Merkens, 1952
Rainbow trout (adult), Salmo gairdneri	1,617 min	Mean survival time	90	Herbert & Merkens, 1952
Rainbow trout (adult), Salmo gairdneri	3,600 min	Mean survival time	80	Herbert & Merkens, 1952
Rainbow trout (adult), Salmo gairdneri	4,441 min	Mean survival time	70	Herbert & Merkens, 1952
Rainbow trout, Salmo gairdneri	48 hrs	LC50	68	Brown, 1968
Rainbow trout (juvenile), Salmo gairdneri	9 days	Weight gain reduced	10	Dixon, 1975
Rainbow trout (juvenile), Salmo gairdneri	4 days	Increased respiration rate	10	Dixon, 1975
Rainbow trout (juvenile), Salmo gairdneri	9 days	Liver damage (necrobiosis)	10	Dixon, 1975
Rainbow trout (yearling), Salmo gairdneri	21 days	65% reduction in weight gain	20	Speyer, 1975

Table 5. (Continued)

Species	Duration	Effect	Result (µg/l)	Reference
Rainbow trout (yearling), Salmo gairdneri	21 days	75% reduction in swimming ability	20	Spoyer, 1975
Rainbow trout (juvenile), Salmo gairdneri	20 days	Abnormal oocyte development	10	Lesniak, 1977
Rainbow trout, Salmo gairdneri	18 days	Production of spermatogonia reduced by 13%	10	Ruby, et al. 1979
Rainbow trout, Salmo gairdneri	18 days	Production of spermatogonia reduced by 50%	30	Ruby, et al. 1979
Atlantic salmon, Salmo salar	58 days	Teratogenic effects to embryos	10	Leduc, 1978
Brook trout (fry), Salvelinus fontinalis	15.2 min	Death	8,640	Karsten, 1934
Brook trout (fry), Salvelinus fontinalis	10.8 min	Death	4,290	Karsten, 1934
Brook trout (fry), Salvelinus fontinalis	11.7 min	Death	2,130	Karsten, 1934
Brook trout (fry), Salvelinus fontinalis	26 min	Death	853	Karsten, 1934
Brook trout (fry), Salvelinus fontinalis	58 min	Death	392	Karsten, 1934
Brook trout (fry), Salvelinus fontinalis	210 min	Death	217	Karsten, 1934
Brook trout (fry), Salvelinus fontinalis	130 hrs	Death	50	Karsten, 1934
Brook trout (fry), Salvelinus fontinalis	27 days	100% survival	20	Karsten, 1934

Table 5. (Continued)

Species	Duration	Effect	Result (µg/l)	Reference
Brook trout (juvenile), Salvelinus fontinalis	3.6 days	Lethal	80	Nell, 1957
Brook trout (juvenile), Salvelinus fontinalis	40 days	Not lethal	50	Nell, 1957
Brook trout (juvenile), Salvelinus fontinalis	25.5 min	75% reduction in swimming endurance	10	Nell, 1957
Brook trout (juvenile), Salvelinus fontinalis	90 days	Reduced growth	33	Koenst, et al. 1977
Brown trout (fry), Salmo trutta	8.2 min	Death	8,030	Karsten, 1934
Brown trout (fry), Salmo trutta	8.9 min	Death	4,140	Karsten, 1934
Brown trout (fry), Salmo trutta	8.2 min	Death	2,070	Karsten, 1934
Brown trout (fry), Salmo trutta	140 min	Death	217	Karsten, 1934
Brown trout (juvenile), Salmo trutta	6.58 min	Geometric mean time to death	1,006	Burdick, et al. 1958
Brown trout (juvenile), Salmo trutta	15 min	Geometric mean time to death	510	Burdick, et al. 1958
Brown trout (juvenile), Salmo trutta	30.1 min	Geometric mean time to death	320	Burdick, et al. 1958
Brown trout (juvenile), Salmo trutta	5 hrs	Oxygen uptake inhibited	25	Carter, 1962
Fathead minnow, Pimephales promelas	48 hrs	LC50	240	Black, et al. 1957
Fathead minnow (juvenile), Pimephales promelas	5 days	LC50	120	Cardwell, et al. 1976

Table 5. (Continued)

Species	Duration	Effect	Result (µg/l)	Reference
Fathead minnow (juvenile), Pimephales promelas	28 days	Reduced growth in length	35	Lind, et al. 1977
Fathead minnow (juvenile), Pimephales promelas	56 days	Reduced growth in length and weight	62	Lind, et al. 1977
Fathead minnow (embryo), Pimephales promelas	96 hrs	LC50	347	Smith, et al. 1978
Fathead minnow (embryo), Pimephales promelas	96 hrs	LC50	272	Smith, et al. 1978
Fathead minnow (embryo), Pimephales promelas	96 hrs	LC50	201	Smith, et al. 1978
Fathead minnow (embryo), Pimephales promelas	96 hrs	LC50	123	Smith, et al. 1978
Fathead minnow (embryo), Pimephales promelas	96 hrs	LC50	186	Smith, et al. 1978
Fathead minnow (embryo), Pimephales promelas	96 hrs	LC50	200	Smith, et al. 1978
Fathead minnow (embryo), Pimephales promelas	96 hrs	LC50	206	Smith, et al. 1978
Black-nosed dace, Rhinichthys atratulus	24 hrs	LC50	220	Lipschuetz & Cooper, 1955
Channel catfish (juvenile), Ictalurus punctatus	26 hrs	LC50	161	Cardwell, et al. 1976
Guppy (juvenile), Poecilia reticulata	120 hrs	Threshold concentration	236	Chen, 1968
Stickleback, Gasterosteus aculeatus	90 min	Depressed respiration rate to 32% of normal	1,040	Jones, 1947
Threespine stickleback (adult), Gasterosteus aculeatus	824 min	Median survival time	134	Broderius, 1973

Table 5. (Continued)

Species	Duration	Effect	Result (µg/l)	Reference
Threespine stickleback (adult), Gasterosteus aculeatus	642 min	Median survival time	170	Broderius, 1973
Threespine stickleback (adult), Gasterosteus aculeatus	412 min	Median survival time	237	Broderius, 1973
Bluegill (juvenile), Lepomis macrochirus	202 min	Median survival time	198	Broderius, 1973
Bluegill (juvenile), Lepomis macrochirus	260 min	Median survival time	194	Broderius, 1973
Bluegill (juvenile), Lepomis macrochirus	351 min	Median survival time	165	Broderius, 1973
Bluegill (juvenile), Lepomis macrochirus	258 min	Median survival time	165	Broderius, 1973
Bluegill (juvenile), Lepomis macrochirus	352 min	Median survival time	144	Broderius, 1973
Bluegill (juvenile), Lepomis macrochirus	655 min	Median survival time	127	Broderius, 1973
Bluegill (juvenile), Lepomis macrochirus	48 hrs	LC50	134	Cardwell, et al. 1976
Bluegill (juvenile), Lepomis macrochirus	48 hrs	LC50	280	Turnbull, et al. 1954
Bluegill (juvenile), Lepomis macrochirus	72 hrs	LC50	154	Doudoroff, et al. 1966
Bluegill (adult), Lepomis macrochirus	48 hrs	LC50	160	Cairns, et al. 1965
Bluegill (adult), Lepomis macrochirus	289 days	Survival reduced	67.8	Kimball, et al. 1978
Bluegill (adult), Lepomis macrochirus	289 days	No reproduction	5.4	Kimball, et al. 1978

Table 5. (Continued)

Species	Duration	Effect	Result (µg/l)	Reference
Smallmouth bass (juvenile), Micropterus dolomieui	7.8 min	Geometric mean time to death	1,980	Burdick, et al. 1958
Smallmouth bass (juvenile), Micropterus dolomieui	12.4 min	Geometric mean time to death	1,430	Burdick, et al. 1958
Smallmouth bass (juvenile), Micropterus dolomieui	15.4 min	Geometric mean time to death	978	Burdick, et al. 1958
Smallmouth bass (juvenile), Micropterus dolomieui	30.6 min	Geometric mean time to death	755	Burdick, et al. 1958
Smallmouth bass (juvenile), Micropterus dolomieui	42.8 min	Geometric mean time to death	478	Burdick, et al. 1958
Smallmouth bass (juvenile), Micropterus dolomieui	80.5 min	Geometric mean time to death	338	Burdick, et al. 1958
Smallmouth bass (juvenile), Micropterus dolomieui	133 min	Geometric mean time to death	243	Burdick, et al. 1958
Smallmouth bass (juvenile), Micropterus dolomieui	290 min	Geometric mean time to death	175	Burdick, et al. 1958
Largemouth bass (juvenile), Micropterus salmoides	2 days	Significant increases in opercular rate	40	Morgan & Kuhn, 1974
Yellow perch (embryo), Perca flavescens	96 hrs	LC50	281	Smith, et al. 1978

Table 5. (Continued)

Species	Duration	Effect	Result (µg/l)	Reference
		SALTWATER SPECIES		
Oyster, *Crassostrea* sp.	10 min	Activity suppression	150	Usuki, 1965
Oyster, *Crassostrea* sp.	3 hrs	Activity inhibition	30,000	Usuki, 1965

REFERENCES

Anderson, P. and L. Weber. 1975. Toxic response as a quantitative function of body size. Toxicol. Appl. Pharmacol. 33: 471.

Black, H.H., et al. 1957. Industrial waste guide--by-product coke. Proc. 11th Ind. Waste Conf. Purdue Univ. 41: 494.

Broderius, S.J. 1970. Determination of molecular hydrocyanic acid in water and studies of the chemistry and toxicity to fish of the nickelocyanide complex. M.S. thesis. Oregon State University, Corvallis.

Broderius, S.J. 1973. Determination of molecular hydrocyanic acid in water and studies of the chemistry and toxicity to fish of metal-cyanide complexes. Ph.D. thesis. Oregon State University, Corvallis.

Broderius, S., et al. 1977. Relative toxicity of free cyanide and dissolved sulfide forms to the fathead minnow, Pimephales promelas. Jour. Fish. Res. Board Can. 34: 2323.

Brown, V.M. 1968. The calculation of the acute toxicity of mixtures of poisons to rainbow trout. Water Res. 2: 723.

Burdick, G.E., et al. 1958. Toxicity of cyanide to brown trout and smallmouth bass. N.Y. Fish Game Jour. 5: 133.

Cairns, J., Jr. and A. Scheier. 1958. The effect of periodic low oxygen upon toxicity of various chemicals to aquatic organisms. Proc. 12th Ind. Waste Conf. Purdue Univ. Eng. Ext. Ser. No. 94, Eng. Bull. 42: 165.

Cairns, J., Jr. and A. Scheier. 1963. Environmental effects upon cyanide toxicity to fish. Notulae Naturae, Acad. Natural Sci., Philadelphia, No. 361.

Cairns, J., Jr., et al. 1965. A comparison of the sensitivity to certain chemicals of adult zebra danios Brachydanio rerio (Hamilton-Buchanan) and zebra danio eggs with that of adult bluegill sunfish Lepomis macrochirus Raf. Notulae Naturae, Acad. Natural Sci., Philadelphia, No. 381.

Cairns, J., Jr., et al. 1976. Invertebrate response to thermal shock following exposure to acutely sub-lethal concentrations of chemicals. Arch. Hydrobiol. 77: 164.

Cardwell, R., et al. 1976. Acute toxicity of selected toxicants to six species of fish. Ecol. Res. Ser. EPA 600/3-76-008. Environ. Res. Lab., U.S. Environ. Prot. Agency, Duluth, MN. 117 p.

Carter, L. 1962. Bioassay of trade wastes. Nature. 196: 1304.

Chen, C.W. 1968. A kinetic model of fish toxicity treshold. Ph.D. thesis. University of California, Berkeley.

Department of Scientific and Industrial Research. 1956. Water pollution research 1955. H.M. Stationery Off. London.

Dixon, D.G. 1975. Some effects of chronic cyanide poisoning on the growth, respiration and liver tissue of rainbow trout. M.S. thesis. Concordia University, Montreal.

Doudoroff, P. 1956. Some experiments on the toxicity of complex cyanides to fish. Sewage Ind. Wastes. 28: 1020.

Doudoroff, P. 1976. Toxicity to fish of cyanides and related compounds: A review. Ecol. Res. Series. EPA 600/3-76-038. Environ. Res. Lab., U.S. Environ. Prot. Agency, Duluth, MN. 154 p.

Doudoroff, P., et al. 1966. Acute toxicity to fish of solutions containing complex metal cyanides, in relation to concentrations of molecular hydrocyanic acid. Trans. Am. Fish. Soc. 95: 6.

Dowden, B.F. and H.J. Bennett. 1965. Toxicity of selected chemicals to certain animals. Jour. Water Pollut. Control Fed. 37: 1308.

Fitzgerald, G.P., et al. 1952. Studies on chemicals with selective toxicity to blue-green algae. Sewage Ind. Wastes. 24: 888.

Henderson, C., et al. 1961. The effects of some organic cyanides (nitriles) on fish. Proc. 15th Ind. Waste Conf. Purdue Univ. Eng. Ext. Ser. No. 106. Eng. Bull. 45: 102.

Herbert, D.W.M. and J.C. Merkens. 1952. The toxicity of potassium cyanide to trout. Jour. Exp. Biol. 29: 632.

Izatt, R.M., et al. 1962. Thermodynamics of metal-cyanide coordination. I. pK, H^{o}, and S^{o} values as a function of temperature for hydrocyanic acid dissociation in aqueous solution. Inorg. Chem. 1: 828.

Jones, J.R.E. 1947. The oxygen comsumption of Gasterosteus aculeatus L. in toxic colutions. Jour. Exp. Biol. 23: 298.

Karsten, A. 1934. Investigations of the effect of cyanide on Black Hills trout. Black Hills Eng. 22: 145.

Kimball, G., et al. 1978. Chronic toxicity of hydrogen cyanide to bluegills. Trans. Am. Fish. Soc. 107: 341.

Koenst, W., et al. 1977. Effect of chronic exposure of brook trout to sublethal concentrations of hydrogen cyanide. Environ. Sci. Technol. 11: 883.

Leduc, G. 1978. Deleterious effects of cyanide on early life stages of Atlantic salmon (Salmo salar). Jour. Fish. Res. Board Can. 35: 166.

Lee, D. 1976. Development of an invertebrate bioassay to screen petroleum refinery effluents discharged into freshwater. Ph.D. thesis. Virginia Polytechnic Inst. State University, Blacksburg.

Lesniak, J.A. 1977. A histological approach to the study of sublethal cyanide effects on rainbow trout ovaries. M.S. thesis. Concordia University, Montreal.

Lind, D., et al. 1977. Chronic effects of hydrogen cyanide on the fathead minnow. Jour. Water Pollut. Control Fed. 49: 262.

Lipschuetz, M. and A.L. Cooper. 1955. Comparative toxicities of potassium cyanide and potassium cuprocyanide to the western blacknosed dace (Rhinichtys atratulus meleagris). N.Y. Fish Game Jour. 2: 194.

Morgan, W.S.G. and P.C. Kuhn. 1974. A method to monitor the effects of toxicants upon breathing rates of largemouth bass (Micropterus salmoides Lacepede). Water Res. 8: 67.

Negilski, D.S. 1973. Individual and combined effects of cyanide pentachlorphenol and zinc on juvenile chinook salmon and invertebrates in model stream communities. M.S. thesis. Oregon State University, Corvallis.

Neil, J.H. 1957. Some effects of potassium cyanide on speckled trout (Salvelinus fontinalis). In: Papers presented at 4th Ontario Ind. Waste Conf. Water Pollut. Adv. Comm., Ontario Water Resour. Comm., Toronto. p. 74-96.

Nelson, E.B. and N.E. Tolbert. 1970. Glycolate dihydrogenase in green algae. Arch. Biochem. Biophys. 141: 102.

Oseid, D. and L. Smith. 1979. The effects of hydrogen cyanide on Asellus communis and Gammarus pseudolimnaeus and changes in their competitive response when exposed simultaneously. Bull. Environ. Comtam. Toxicol. 21: 439.

Patrick, R., et al. 1968. The relative sensitivity of diatoms, snails, and fish to twenty common constituents of industrial wastes. Prog. Fish-Cult. 30: 137.

Roback, S.S. 1965. Environmental requirments of Trichoptera. In: Biological problems in water pollution. 3rd Seminar (1962), R.A. Taft Sanit. Eng. Center, Cincinnati, Ohio. p. 118-126.

Ruby, S.M., et al. 1979. Inhibition of spermatogensis in rainbow trout during chronic cyanide poisoning. Arch. Environ. Contam. Toxicol. 8: 533.

Smith, L.L., Jr., et al. 1978. Acute toxicity of hydrogen cyanide to freshwater fishes. Arch. Environ. Contam. Toxicol. 7: 325.

Smith, L.L., Jr., et al. 1979. Acute and chronic toxicity of HCN to fish and invertebrates. Ecol. Res. Ser. EPA-600/3-79-009. Environ. Res. Lab., U.S. Environ. Prot. Agency, Duluth, MN. 115 p.

Speyer, M.R. 1975. Some effects of chronic combined arsenic and cyanide poisning on the physiology of rainbow trout. M.S. thesis. Concordia University, Montreal.

Turnbull, H., et al. 1954. Toxicity of various refinery materials to freshwater fish. Ind. Eng. Chem. 46: 324.

U.S. EPA. 1980a. Unpublished laboratory data. Environ. Res. Lab., Duluth, Minnesota.

U.S. EPA. 1980b. Unpublished laboratory data. Environ. Res. Lab., Narragansett, Rhode Island.

Usuki, I. 1965. A comparison of the effects of cyanide and azide on the ciliary activity of the oyster gill. Sci. Rep. Tohoku University, Fourth Sci. 22: 137.

Wallen, I.E., et al. 1957. Toxicity to Gambusia affinis of certain pure chemicals in turbid waters. Sewage Ind. Wastes. 29: 695.

Webster, D.A. and D.P. Hackett. 1965. Respiratory chain of colorless algae. I. Chlorophyta and Euglenophyta. Plant Physiol. Lancaster. 40: 1091.

Mammalian Toxicology and Human Health Effects

INTRODUCTION

Cyanides are defined as hydrogen cyanide (HCN) and its salts. The toxicological effects of cyanides are based upon their potential for rapid conversion by mammals to HCN. Various organic compounds containing the cyanide (CN) moiety which may have a potential for conversion to HCN *in vivo* will not be considered in this document. Cyanides have long been feared for their high lethality and their fulminating action. At the present time, however, cyanides do not constitute an important or widespread environmental health problem. Almost all examples of human cyanide poisoning or adverse environmental effects in the past have involved occupational exposures or relatively localized sources of pollution. Cyanides are uncommon in U.S. water supplies and in the atmosphere. Although some food plants clearly can cause acute cyanide poisoning if ingested in sufficient amount, the evidence associating cyanide compounds in other plants with chronic neuropathies is not convincing.

Some evidence suggests that the uses of cyanide in the U.S. are increasing, and, therefore, continued vigilance in the form of monitoring is indicated. However, a number of properties and characteristics of cyanide indicate that it will probably remain only a potential pollutant or one of secondary concern. For example, cyanide has a low degree of persistence in the environment, and it is not accumulated or stored in any mammalian species that has been studied. In keeping with the latter, a sizeable body of

experimental evidence suggests that cyanide has an unusually low degree of chronic toxicity. It does not appear to be mutagenic, teratogenic, or carcinogenic.

No new evidence was encountered to suggest that the Public Health Service (PHS) drinking water standard for cyanide set in 1962 should be lowered (National Institute Occupational Safety Health (NIOSH), 1976).

EXPOSURE

The toxicological effects of cyanides are based upon their potential for rapid conversion by mammals to HCN.

Cyanide production in the U.S. is now over 700 million pounds per year and appears to be increasing steadily (Towill, et al. 1978). The sources and industrial uses of cyanide compounds in the United States have recently been reviewed exhaustively (NIOSH, 1976; Towill, et al. 1978). Briefly, the major industrial users of cyanide in the U.S. are the producers of steel, plastics, synthetic fibers and chemicals, and the electroplating and metallurgical industries. In addition to these industries (see Table 1), cyanide wastes are discharged into the environment from the pyrolysis of a number of synthetic and natural materials and from chemical, biological, and clinical laboratories. Although wool, silk, polyacrylonitrile, nylon, polyurethane, and paper are all said to liberate HCN on combustion, the amounts vary widely with the conditions. As yet there is no standardized fire toxicity test protocol in the U.S. (Terrill, et al. 1978).

Despite numerous potential sources of pollution, cyanide is relatively uncommon in most U.S. water supplies. A survey of 969

TABLE 1

Inorganit Cyanide Wastes*

Source and Material	Bureau of the Census regions									Total
	I	II	III	IV	V	VI	VII	VIII	IX	
Annual waste production (lb/year)										
Cyanides from electroplating	2.78×10^6	6.07×10^6	6.86×10^6	0.96×10^6	1.04×10^6	0.49×10^6	0.77×10^6	0.15×10^6	2.20×10^6	21.32×10^6
Paint sludge										
cyanides	1,000	9,900	13,800	2,900	3,850	2,150	3,350	550	7,300	44,900
sludge	0.92×10^6	8.12×10^6	11.32×10^6	2.40×10^6	3.16×10^6	1.76×10^6	2.74×10^6	0.44×10^6	5.97×10^6	36.83×10^6
Paint residue										
cyanides	0.18×10^5	0.57×10^5	0.62×10^5	0.23×10^5	0.47×10^5	0.20×10^5	0.30×10^5	0.13×10^5	0.41×10^5	3.11×10^5
old paint	13×10^6	41×10^6	44×10^6	16×10^6	34×10^6	14×10^6	21×10^6	9×10^6	29×10^6	221×10^6
Stored wastes (lb)										
Sodium cyanide		1,400						16		1,416
Calcium cyanide							180		25	205
Copper cyanide		100						32		132
Potassium cyanide					2					2
Silver cyanide								16	10	26
Potassium ferricyanide					4					4
Potassium ferrocyanide						12				12

*Source: Ottinger, et al. 1973.

U.S. public water supply systems in 1970 revealed no cyanide concentrations above the mandatory limit (McCabe, et al. 1970). In 2,595 water samples, the highest cyanide concentration found was 8 ppb and the average concentration was 0.09 ppb (Towill, et al. 1978). In part, this must be ascribed to the volatility of undissociated hydrogen cyanide which would be the predominant form in all but highly alkaline waters. Also, in part, cyanide ion would have a decided tendency to be "fixed" in the form of insoluble or undissociable complexes by trace metals. Cyanide may complex irreversibly with heavy metals in water supplies and thereby be biologically inactivated in terms of toxicity attributable to cyanide. Conversely, some cyanide complexes, such as nitroprusside, are readily dissociable and elicit toxic responses directly attributable to the release of cyanide in vivo. In view of the increased production and uses of cyanide in the U.S., however, continued vigilance in the form of monitoring is certainly indicated, particularly in the proximity of known potential sources of pollution. Techniques for monitoring have been reviewed elsewhere (NIOSH, 1976; Towill, et al. 1978).

Ingestion from Water

As noted above, cyanide is an uncommon pollutant in most U.S. water supplies, and documented examples of levels in excess of the 1962, U.S. Public Health Service limits (U.S. PHS, 1962) are extremely rare. No human cases of illness or death due to cyanide in water supplies are known. The lack of such documentation, of course, cannot be accepted complacently. It is entirely possible that pulse discharges of industrial wastes result in high localized

concentrations which have escaped detection, but general recognition of the high toxicity of cyanide has made its removal standard practice in most industries (Reed, et al. 1971). Fortunately, known methods for cyanide removal including alkaline chlorination, hypochlorite treatment, reaction with aldehydes, electrolytic decomposition, exposure to ionizing radiation, and heating are effective and relatively economical (Lawes, 1972; Watson, 1973).

A few accidents have resulted in massive fish kills, some livestock deaths, and environmental damage. Cyanide, unknowingly released from a sewage plant in Oak Ridge, Tenn., was responsible for the death of 4,800 fish in Melton Hill Lake near the sewage outfall (The Oak Ridger, 1975). About 1,500 drums (30 and 55 gallon) containing cyanides disposed of near Byron, Illinois resulted in long-range environmental damage and livestock death. Surface water runoff from the area contained up to 365 ppm cyanide (Towill, et al. 1978).

Ingestion from Food

Except for certain naturally occurring organonitriles in plants, it is uncommon to find cyanide in foods in the U.S. Additionally, there is no data available indicating bioconcentration of cyanide. The U.S. EPA Duluth laboratory states that the bioconcentration factor will be very close to zero (Stephan, 1980). For criterion calculation purposes, however, a tissue content approaching that of the surrounding medium is assumed. In higher plants the major group of organonitriles are the cyanogenic glycosides, and at least 20 distinct compounds are known. Perhaps the best known of this group is the compound amygdalin, which is found in

many parts of the cherry laurel and the seeds of cherries, plums, peaches, apricots, apples, and pears. Amygdalin is the chief ingredient in Laetrile. Both Laetrile and amygdalin-containing fruit pits have been implicated as causes of acute cyanide poisoning in humans (Braico, et al. 1979; Gosselin, et al. 1976). The release of free cyanide from cyanogenic glycosides can be effected by acid hydrolysis or most rapidly by β-glucosidases, enzymes present in plants and in the intestinal microflora of mammals but found in only trace amounts in animal tissues (Conchie, et al. 1959).

Another naturally occurring group of organonitriles are called the pseudocyanogenic glycosides of which the best known example is cycasin from the Cycadaceae. As implied by the name, cyanide release from these compounds is unlikely to occur in vivo since alkaline hydrolysis is required (Miller, 1973). Cycasin and related glycosides are highly toxic and their ingestion along with foodstuffs has been implicated in a variety of so-called "tropical neuropathies" and amblyopias (Osuntokun, 1968). Although these neurological disturbances have frequently been cited in the literature (Towill, et al. 1978) as examples of "chronic cyanide poisoning," the evidence for that extrapolation is indirect and inconclusive. The failure of repeated attempts to produce similar syndromes with pure hydrogen cyanide or its salts (see following discussion), strongly suggests that the neuropathies produced by cycasin-containing foods are due to other unrecognized toxins, to the cycasin per se, or to uncharacterized toxic metabolites, rather than to cyanide.

Other organonitriles found in plants include the lathyrogenic compounds, such as α-glutamyl-β-cyanoalanine, the glucosinolates such as glucobrassicin, and the cyanopyridine alkaloids such as ricinine and indoleacetonitrile (Towill, et al. 1978). Although many of these are toxic to mammals, no evidence links their toxicity to cyanide poisoning.

Inhalation

Hydrogen cyanide vapor is absorbed rapidly through the lungs (Gettler and St. George, 1934). Because HCN has a pKa of 9.2 and exists primarily as the acid under biological conditions, absorption across the alveolar membrane should be rapid (Wolfsie and Shaffer, 1959). Human inhalation of 270 ppm HCN vapor brings death immediately, while 135 ppm is fatal after 30 minutes (Dudley, et al. 1942).

Cyanide absorption following inhalation of very low concentrations is indicated by the observation that smokers have higher thiocyanate levels in plasma and other biological fluids than do nonsmokers (Wilson and Matthews, 1966). Cyanide levels usually are not significantly different in smokers as compared with nonsmokers (Pettigrew and Fell, 1973; Wilson and Matthews, 1966), since cyanide absorbed from inhaled tobacco smoke is rapidly converted to thiocyanate (Johnstone and Plimmer, 1959; Pettigrew and Fell, 1973). Inhalation of cyanide salt dusts is also dangerous because the cyanide will dissolve on contact with moist mucous membranes and be absorbed into the bloodstream (Davison, 1969; Knowles and Bain, 1968).

The so-called distinctive odor of bitter almonds ascribed to HCN does not necessarily serve as a warning of exposure. The ability to smell hydrogen cyanide appears to be a genetically determined trait. Individuals vary widely from being unable to detect the odor to being extremely sensitive to it (Kirk and Stenhouse, 1953).

Dermal

Hydrogen cyanide, in either liquid or vapor form, is absorbed through the skin (Drinker, 1932; Potter, 1950; Tovo, 1955; Walton and Witherspoon, 1926). Absorption is probably increased if the skin is cut, abraded, or moist. Many accidents involving skin contamination also involve inhalation exposure; the contribution due to skin absorption in these cases is difficult to assess. Potter (1950) described a case in which liquid HCN ran over the bare hand of a worker wearing a fresh air respirator. Cyanide inhalation was prevented, but the worker collapsed into deep unconsciousness within five minutes, suggesting significant percutaneous absorption.

PHARMACOKINETICS

Absorption

Probably the common commercial inorganic cyanides are rapidly absorbed from the stomach and duodenum. Certainly, the human experience in regard to the rapidly lethal effects (Gosselin, et al. 1976) of ingested cyanides is in accord with the above, but experimental studies which actually define quantitatively the rates of penetration are not available.

Hydrogen cyanide is a weak acid with a pKa of 9.2. Thus, the acid milieu of the stomach would greatly favor the undissociated

species, HCN, which should further hasten absorption. Even at the physiological pH of 7.4, however, cyanide would exist predominantly as the unionized moiety which would serve to facilitate its transfer among various body compartments (see previous discussion). In accord with the theory of nonionic diffusion cyanide would be predicted to accumulate in body compartments which are at a higher pH (more alkaline) than blood. At present, no evidence can be cited to substantiate directly that prediction.

It has long been common knowledge that hydrogen cyanide gas or vapors are rapidly absorbed via the lungs, producing reactions within a few seconds and death within minutes (Gosselin, et al. 1976). Hydrogen cyanide has been used as the instrument of execution for convicted criminals in some states of the U.S. primarily because of its rapid lethal effects on inhalation of high concentrations.

Hydrogen cyanide gas or solutions are absorbed through the intact skin much more readily than are the ionized salts which are less lipid soluble (Wolfsie and Shaffer, 1959). Absorption is probably increased in both cases if the skin has been cut or abraded. Alleged cases of human skin absorptions, however, are often complicated by the possibility of concomitant inhalation of cyanide gas. Again, quantitative estimates of the rate of penetration of skin by various forms of cyanide are not available.

Distribution

Cyanide is distributed to all organs and tissues via the blood, where its concentration in red cells is greater than that in plasma by a factor of two to three. Presumably, the accumulation

of cyanide in erythrocytes is a reflection of its binding to methemoglobin. Methemoglobin is found normally in the blood of nonsmokers at concentrations as high as 2 percent of the total circulating pigment (Smith and Olson, 1973). However, there may be other factors as yet unrecognized which favor the accumulation of cyanide in red cells. Cyanide may also accumulate locally in body cells because of binding to metalloproteins or enzymes such as catalase or cytochrome c oxidase (Smith, et al. 1977). The possibility of concentration differences due to pH gradients between body compartments was mentioned above. Certainly, one would predict that cyanide would readily cross the placenta, but again quantitative data are lacking.

Metabolism

By far, the major pathway for the metabolic detoxication of cyanide involves its conversion to thiocyanate via the enzyme rhodanese (de Duve, et al. 1955). Rhodanese is widely distributed in the body, but the highest activity is found in mammalian liver (Table 2). The rate of the rhodanese reaction *in vivo* is limited by the availability of the endogenous sulfur-containing substrate, the identity of which is still unknown. Thiosulfate can serve as a substrate for rhodanese with a high degree of efficiency both *in vivo* and *in vitro* (Chen and Rose, 1952; Himwich and Saunders, 1948).

Alternative minor metabolic pathways for cyanide metabolism include conjugation with cysteine to form 2-iminothiazolidene-4-carboxylic acid, a reaction that is said to proceed nonenzymatically (Figure 1). In rats given a total dose of 30 mg over an

TABLE 2

Rhodanese Activity In Tissues Of The Dog, Rhesus Monkey, Rabbit, And Rat[a]
(mg CN converted to SCN^- per gram of tissue)

Tissue	Dog		Rhesus Monkey		Rabbit		Rat	
	Range[a]	Number of observations	Range[a]	Number of observations	Range	Number of observations	Range	Number of observations
Suprarenals								
whole	2.14-3.60 (5.46, 4.50)	6	0.14-1.35	3	1.24-3.94	2	0.27-0.41	2
cortex	2.86-5.62	2						
medulla	0.27-1.12	2						
Liver	0.78-1.46 (4.91, 6.28)	7	10.98-15.16 (5.98)	4	7.98-18.92	9	14.24-28.38	9
Brain								
cortex	0.34-0.92	7	0.27	1	1.41-1.44	2	0.70-0.72	2
caudate nucleus	0.27-1.06	7	0.34-0.50	2	0.13-0.18	2		
midbrain	0.52-1.35	6	0.22-0.80	2	1.17-1.39	2	0.73-1.13	2
cerebellum	0.21-1.22	7	0.33	1	0.63-1.24	2		
medulla	0.38-1.52	7	0.49-0.85	2	0.91	1		
Spinal cord								
cervical	0.15-1.08	7	0.56-0.57	2	0.89-0.90	2	0.16-0.18	2
lumbar	0.12-0.84	4	0.20-0.42	2	0.35-1.74	2	0.23-0.27	2
sacral	0.16-1.41	4	0.23-0.28	2	0.59-1.10	3	0.56-0.74	2
Heart	0.11-0.14	6	0.48-0.82	3				
Kidney	0.42-0.74	6	2.46-3.58	4	6.20-7.69	3	10.44-11.08	2
Testes	0.32-0.41	5	0.38-0.46	3	0.32-0.36	2	1.24-1.61	2
Epididymis	0.29	1						
Ovaries	0.42	1						
Lung	0.16-0.17	3	0.11-0.21	2	0.30	1		
Spleen	0.10-0.14	2	0.12-0.34	2	0.40	1		
Muscle	0.03-0.19	6	0.23-0.57	3	0.20	1		
Intestine					0.18	1		
duodenum	0.05-0.11	3						
jejunum	0.04	1						
Eye	0.02	1						
Optic nerve	0.35	1						

TABLE 2 (Cont.)

Tissue	Dog		Rhesus Monkey		Rabbit		Rat	
	Range[a]	Number of observations	Range[a]	Number of observations	Range	Number of observations	Range	Number of observations
Salivary gland, parotid	0.05-0.36	3	0.99	1				
Lymph node	0.08-0.13	2						
Pancreas	0.14-0.28	4	0.12-0.44	2				
Thyroid	0.05-0.94	3						
Anterior pituitary	.26	1						
Whole blood	0.01-0.02	2						
Erythrocytes	0.01-0.02	2						
Plasma	0.01	1						

[a]Figures in parentheses are single observations falling outside the normal range.

*Source: Adapted from Himwich and Saunders, 1948.

NITRILES

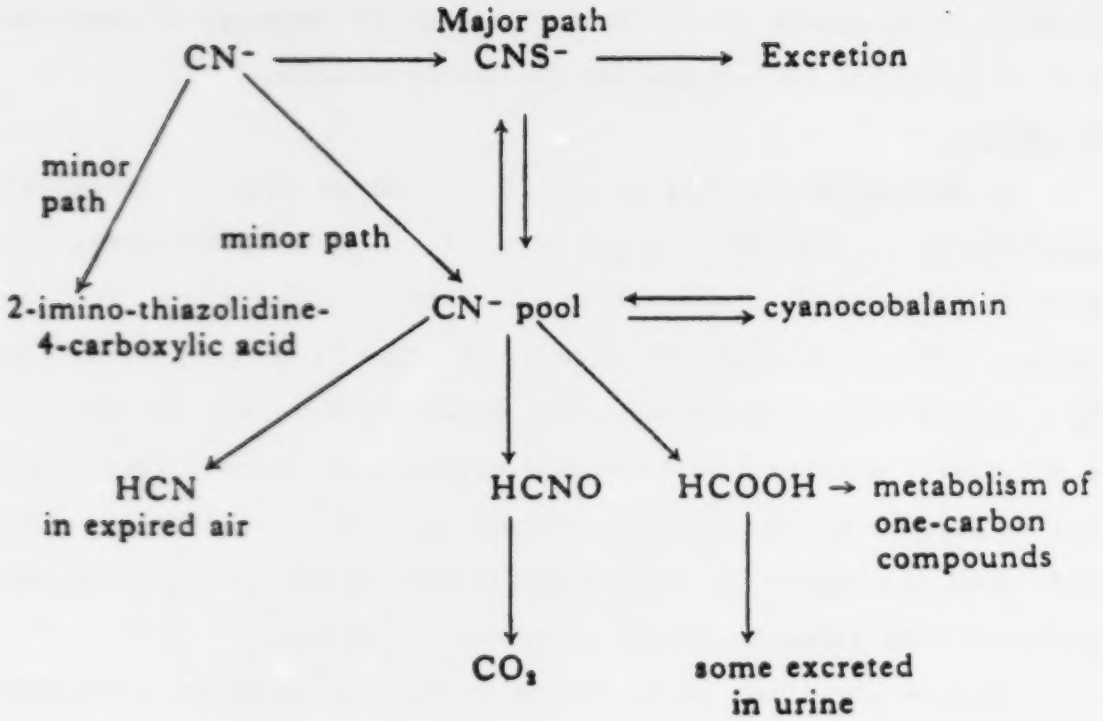

FIGURE 1

Fate of Cyanide Ion in the Body

Source: Williams, 1959

eight-day period, this pathway accounts for no more than 15 percent of the total cyanide (Wood and Cooley, 1956). A very small fraction of the total cyanide is bound by hydroxocobalamin, probably less than 1 percent (Brink, et al. 1950). A small amount (about 1 to 2 percent) is excreted unchanged as HCN via the lungs (Friedberg and Schwarzkopf, 1969). By reactions that are not well understood, cyanide gains access to metabolic pathways for one-carbon compounds and is converted to formate and to carbon dioxide.

Excretion

As estimated in rats given 30 mg sodium cyanide intraperitoneally over a period of eight days, 80 percent of the total cyanide is excreted in the urine in the form of thiocyanate (Wood and Cooley, 1956). Because the fate of cyanide is largely determined by a single metabolic pathway, one would predict that it would fit a relatively simple pharmacokinetic model, e.g., first order kinetics in plasma, but such detailed analyses have not been made. Cyanide does not appear to accumulate significantly in any body compartment with repeated doses or chronic exposures.

Because the liver contains the highest activity of rhodanese, it is possible that pre-existing liver disease might slow the rate of cyanide metabolism, but no studies appear to address this question. No inhibitors of rhodanese are known which are active *in vivo*.

EFFECTS

Acute, Subacute, and Chronic Toxicity

Hydrogen cyanide and its alkali metal salts are chemicals of high inherent lethality to man and other mammals. The mean lethal

dose of these substances by mouth in human adults is in the range of 50 to 200 mg (1 to 3 mg/kg), and death is rarely delayed more than an hour (Gosselin, et al. 1976). In respiratory exposures to hydrogen cyanide gas, death occurs in 10 to 60 minutes at approximate ambient concentrations of 0.1 to 0.3 mg/l (or 100 to 300 ppm) (Table 3). In nonfatal poisonings recovery is generally rapid and complete.

The acute effects of cyanide poisoning in all obligate aerobic species can be ascribed directly or indirectly to a single specific biochemical lesion, namely the inhibition of cytochrome c oxidase (Gosselin, et al. 1976). Inhibition of this terminal enzyme complex in the respiratory electron transport chain of mitochondria impairs both oxidative metabolism and the associated process of oxidative phosphorylation (Lehninger, 1975). The ensuing syndrome has been well characterized in man and in laboratory animals (Gosselin, et al. 1976). In its major features cyanide poisoning resembles the effects of acute hypoxia whether the latter is due to airway obstruction or to the absence of oxygen (anoxic hypoxia), carbon monoxide poisoning (anemic hypoxia), or shock (stagnant or hypokinetic hypoxia), all of which result in a decreased supply of oxygen to peripheral tissues.

Cyanide poisoning differs from other types of hypoxia in that the oxygen tension in peripheral tissues usually remains normal or may even be elevated (Brobeck, 1973). This paradoxical difference arises because the effect of cyanide is to block the utilization of oxygen by aerobic cells, a novel condition referred to as histotoxic hypoxia. The organ systems most profoundly affected,

TABLE 3

Human Response To Inhaled Cyanide And Cyanide-Containing Compounds

Compound	Cyanide concentration (mg/liter)	Cyanide concentration (ppm)	Response	Reference
Hydrogen cyanide	0.3	270	Immediately fatal	Prentiss, 1937
	0.2	181	Fatal after 10-min exposure	Prentiss, 1937
	0.15	135	Fatal after 30-min exposure	Prentiss, 1937
	0.12-0.15	110-135	Fatal after ½ to 1 hr or later, or dangerous to life	Fassett, 1963
Cyanogen		16	Nasal and eye irritation after 6 to 8 min	McNerney and Schrenk,1960
Cyanogen chloride	0.40	159	Fatal after 10-min exposure	Prentiss, 1937
	0.120	48	Fatal after 30-min exposure	Fassett, 1963
	0.005	2	Intolerable concentration, 10-min exposure	Fassett, 1963
	0.0025	1	Lowest irritant concentration, 10-min exposure	Fassett, 1963
Cyanogen bromide	0.40	92	Fatal after 10-min exposure	Prentiss, 1937
	0.035	8	Intolerable concentration	Prentiss, 1937
	0.006	1.4	Greatly irritating to conjunctiva and the mucous membranes of the respiratory system	Prentiss, 1937

however, are the same as those impaired in any hypoxia irrespective of etiology, namely the brain and the heart because of their high dependence on oxidative metabolism. Two signs associated with cyanide poisoning in man (Gosselin, et al. 1976) follow from the preceding: (1) the failure to utilize molecular oxygen in peripheral tissues results in abnormally high concentrations of oxyhemoglobin in the venous return which accounts for a flush or brick-red color of the skin; and (2) attempts to compensate for the inhibition of oxidative metabolism leads to increased demands on glycolysis which accounts for a metabolic (lactic) acidosis.

A special but less unique effect of cyanide is stimulation of the chemoreceptors of the carotid body which elicits a characteristic pattern of reflex activity (Heymans and Neil, 1958). Since the nature of these chemoreceptors is unknown, it is possible that the effect of cyanide on them is due also in some way to the inhibition of cytochrome c oxidase. Stimulation of the carotid body chemoreceptors by cyanide results in an immediate, well-sustained, and marked augmentation of the respiration. Circulatory effects which often accompany the increase in ventilation include a transient rise in blood pressure which is probably secondary to a reflex sympathetic discharge. The rise in blood pressure is often accompanied by a bradycardia which some authorities insist is not due to the common baroreceptor reflex via the vagus nerves. The pressor response is followed by a fall in blood pressure to hypotensive levels from which the victim may not recover (Heymans and Neil, 1958).

The other prominent effect of cyanide on the respiration is a direct depression or fatal arrest which is the result of an action of cyanide at the level of the brain stem nuclei responsible for the control of breathing. In poisoned victims, the heart beat invariably outlasts breathing movements. The cardiac irregularities often noted may be secondary to respiratory embarrassment, but direct histotoxic effects of cyanide on myocardial cells are an even more likely mechanism.

Massive oral doses or concentrated respiratory exposures may result in a sudden unconsciousness which may simply represent fainting secondary to the delayed drop in blood pressure noted previously. Presumably, the histotoxic hypoxia triggers a massive peripheral vasodilation resulting in orthostatic hypotension and collapse. The sequence of events is slower on exposure to lower concentrations (Table 3) and victims may experience anxiety, confusion, vertigo, and giddiness before loss of consciousness. Unconsciousness is followed by asphyxial convulsions which may be violent and generalized. Opisthotonus, trismus, and incontinence are common. The seizures may be followed by a brief period of paralysis or rigidity and by death from apnea (Gosselin, et al. 1976).

Despite the high lethality of large single doses or acute respiratory exposures to high vapor concentrations of cyanide, repeated sublethal doses do not result in cumulative adverse effects. Thus, cyanide is an example of a chemical which has a high acute toxicity, but an unusually low degree of subacute or chronic toxicity. Hertting, et al. (1960) administered doses (0.5 to 2 mg/kg) of sodium cyanide once or twice each day to dogs. This usually

resulted in acute toxic signs from which the animals recovered completely within half an hour. This regimen was continued over a period of 15 months with no evident pathophysiologic changes in organ function or permanent alteration in intermediary metabolism. Similarly, rats tolerated the equivalent of an acute oral LD_{50} of potassium cyanide each day for 25 days when it was mixed with their regular diet (Hayes, 1967).

Workers at American Cyanamid (1959) fed to beagle dogs a diet containing 150 ppm sodium cyanide for 30 days without observing a significant effect on their food consumption, hematologic parameters, behavioral characteristics, or microscopic changes in their organs or tissues. Howard and Hanzal (1955) fed a diet that had been fumigated with cyanide gas and contained the equivalent of 100 to 300 ppm hydrogen cyanide to rats for two years, also with essentially negative findings. The conclusion seems inescapable that cyanide, in substantial but sublethal intermittent doses, can be tolerated for long periods of time and perhaps indefinitely.

It seems reasonable to assume that continuous exposure to some as yet undefined, but low concentration of hydrogen cyanide gas, could lead inevitably to an exhaustion of the reserve capacity of mammals to inactivate and detoxify cyanide. The rate at which cyanide can be inactivated during acute exposure has been measured in guinea pigs. By continuously infusing cyanide solutions intravenously at different rates, Lendle (1964) showed that at a rate of 0.076 $mg/kg^{-1}/min^{-1}$ about 90 percent of the single lethal dose as determined by "bolus" injection could be detoxified over the course of an hour. When the rate of administration was slowed, multiple

lethal doses could be tolerated. Extrapolation to a dose rate that could be tolerated indefinitely, however, does not seem justified with such a highly artificial model system.

Synergism and/or Antagonism

Since cyanide acts by inhibiting cytochrome c oxidase, it is reasonable to presume that any other established inhibitor of the same enzyme would have toxic effects synergistic with (or additive to) those of cyanide. An established example of such a substance is sulfide which is encountered as hydrogen sulfide gas or as the alkali metal salts (Smith and Gosselin, 1979). Sulfide is even more potent than is cyanide as an inhibitor of cytochrome c oxidase, and similarities between sulfide and cyanide inhibition suggest that they act by similar mechanisms (Nicholls, 1975; Smith, et al. 1977). No specific experimental studies can be cited, however, on the combined effects of cyanide and sulfide in either *in vitro* or *in vivo* systems.

The only other established inhibitor of cytochrome c oxidase is azide (given either as hydrazoic acid or its alkali metal salts). Azide is a much weaker inhibitor of cytochrome c oxidase than is cyanide or sulfide, and it appears to act by a different inhibitory mechanism (Smith, et al. 1977). Again, no specific studies can be cited to establish whether azide has synergistic or additive effects in combination with cyanide.

Although cyanide produces the cellular equivalent of hypoxia, there is no reason to suppose that other causes of hypoxia would have effects additive to or synergistic with those of cyanide. By coincidence one cause of anemic hypoxia (Brobeck, 1973), namely,

methemoglobinemia, is a specific antagonist to cyanide (see following). Oxygen has no effect on cyanide inhibition of cytochrome c oxidase *in vitro*, and it does not reverse the course of cyanide poisoning *in vivo*. Since cyanide blocks the utilization of molecular oxygen in peripheral tissues, its effects on oxygen tension are opposite in direction to those of "true" hypoxia. Since cytochrome c oxidase has a very high affinity for molecular oxygen, it seems unlikely that the oxygen tension in peripheral tissues in cyanide poisoning is ever a limiting parameter.

Cyanide poisoning is specifically antagonized by any chemical agent capable of rapidly generating methemoglobin *in vivo* such as sodium nitrite, hydroxylamine, amyl nitrite, and a large number of aromatic amino- and nitro-compounds such as aniline, p-aminopropiophenone, and nitrobenzene (Smith and Olson, 1973). Methemoglobin binds cyanide tightly in the form of the biologically inactive complex, cyanmethemoglobin. From a therapeutic standpoint there are several disadvantages to the induction of methemoglobinemia despite its established efficacy. Cyanmethemoglobin is a dissociable complex, and eventually the dissociation of free cyanide from it may result in a recurrence of symptoms. The procedure is limited by the concentration of methemoglobin that can be tolerated by the victim, and the chemicals used to generate methemoglobin have toxic side effects of their own (Gosselin, et al. 1976).

A second therapeutically useful approach to the antagonism of cyanide poisoning is to provide an exogenous substrate for the enzyme rhodanese, which converts cyanide to the considerably less toxic form of thiocyanate. The endogeneous substrate for rhodanese

is not known, but p-toluene thiosulfonate ($CH_3C_6H_4$-SO_2-S^-)is 4.5 times more active than thiosulfate as a substrate in vitro (Sorbo, 1953). Ethyl thiosulfate (C_2H_5-S-SO_3-0^-), ethyl xanthate ($C_2H_5OCS_2^-$), diethyl dithiocarbamate ($(C_2H_5)_2NCS_2^-$), hydrosulfite ($S_2O_4^=$) and colloidal sulfur are all inactive as substrates for rhodanese (Sorbo, 1953). It is probable that other sulfur compounds as yet untested can also serve as substrates for rhodanese.

A variety of cobalt compounds effectively antagonize cyanide poisoning, presumably by reacting chemically with free cyanide, e.g., cobaltous chloride, hydroxocobolamine, and cobalt EDTA. The latter two compounds have been used in humans (Gosselin, et al. 1976). Although oxygen alone has no effect on cyanide poisoning, it is said to potentiate the anti-cyanide actions of thiosulfate and particularly the thiosulfate-nitrite combination (Way, et al. 1966).

Teratogenicity, Mutagenicity, and Carcinogenicity

Data are not available on teratogenic, mutagenic, or carcinogenic effects of cyanide, nor do there appear to be any published studies with analagous compounds from which one might postulate the possible adverse effects of long-term, low-level exposure. As previously indicated, a number of studies designed to show chronic or cumulative adverse effects yielded only negative findings. It is possible that cyanide has anti-neoplastic activity; at least one study (Perry, 1935) reported a low therapeutic index for cyanide against rat sarcomas.

In contrast, thiocyanate, the major product of cyanide detoxification in vivo, has produced developmental abnormalities in the

chick (Nowinski and Pandra, 1946) and ascidian embryo (Ortolani, 1969) at high concentrations. Unfortunately, these studies with thiocyanate cannot be extrapolated to man, nor can those of Hrizu, et al. (1973), who reported a cytostatic effect of thiocyanate on human KB cells in culture as well as an increased survival rate in mice inoculated with Ehrlich ascites tumor cells. Again, the amounts used preclude any meaningful extrapolation to human patients. Thus, there is no evidence that chronic exposure to cyanide results in teratogenic, mutagenic, or carcinogenic effects.

CRITERION FORMULATION

Existing Guidelines and Standards

The U.S. Public Health Service Drinking Water Standards of 1962 established 0.2 mg CN^-/l as the acceptable criterion for water supplies. In addition to defining the 0.2 mg/l criterion for cyanide, the PHS set forth an "objective" to achieve concentrations below 0.01 mg CN^-/l in water "because proper treatment will reduce cyanide levels to 0.01 mg/l or less" (U.S. PHS, 1962). The Canadian government has adopted criterion and objective concentrations of 0.2 mg CN^-/l and 0.02 mg CN^-/l, respectively. The latter figure represents the lower limit of detection by colorimetric methods (Health and Welfare, Canada, 1977).

The U.S. PHS criterion was based on cyanide toxicity to fish and not to man. Obviously, a disparity exists between the exposure condition for man and for fish. The cited human experience involved discrete single doses by mouth whereas the fish data are derived from continuous total body exposure. The latter conditions are not a very realistic model from which to assess the human hazard. Even chronic occupational exposures of men to hydrogen cyanide gas allows for respite at the end of each working day.

Current Levels of Exposure

Since cyanide is encountered only infrequently in water supplies or in the atmosphere and since long-term and large-scale monitoring has not been conducted, insufficient data exist to estimate current levels of exposure of the general population. A number of factors contribute to the rapid disappearance of cyanide from water. Bacteria and protozoa may degrade cyanide by converting it to

carbon dioxide and ammonia (Leduc, et al. 1973). Cyanide is converted to cyanate during chlorination of water supplies (Rosehart and Chu, 1974). An alkaline pH favors the oxidation by chlorine, whereas an acid pH favors volatilization of HCN into the atmosphere. As cited, cyanide concentrations above 8 ppb were not found in a survey of 2,595 water samples collected throughout the United States (Towill, et al. 1978). Thus, these concentrations were well below the objective levels established by the PHS.

Special Groups at Risk

Although it was speculated that the elderly and the debilitated individuals in our population may be at special risk with respect to cyanide, no experimental or epidemiological studies can be cited to prove the point.

Basis and Derivation of Criteria

As shown in Table 4, the criterion of 0.2 mg CN^-/l (200 µg/l) allows for safety factors ranging from 41 to 2,100. El Ghawabi, et al. (1975) studied the effects of chronic cyanide exposure in the electroplating sections of three Egyptian factories. A total of 36 male employees with exposures up to 15 years were studied and compared with a control group of 20 normal, nonsmoking males. Only minimal differences with respect to thyroid gland size and function were found. The El Ghawabi study was given considerable weight in formulating the NIOSH recommendations for occupational exposure which gives a safety factor of 41 when applied to drinking water by the usual extrapolations (Table 4). Finally, a safety factor of 2,100 is obtained using the results of a two-year chronic feeding study in rats. When fed at the rate of 12 mg/kg per day over the

TABLE 4

Basis and Derivation of Cyanide Criterion

Exposure Levels[a]	Route	Species	Calculated Daily Exposure	Margin of Safety[d]	Investigator
9.2 mg/m^3	Inhalation	Man	60.8 mg[b]	152	El Ghawabi, et al. 1975
2.5 mg/m^3	Inhalation	Man	16.5 mg[b]	41	NIOSH, 1976
12 mg/kg	Oral	Rat	840 mg[c]	2100	Howard and Hanzal, 1955

[a] NOAEL

[b] Based on 100% retention and on alveolar exchange of $6.6m^3$ for 8 hours.

[c] Rat data converted to human equivalent assuming food consumption of 60 g/kg for rats and 70 kg human.

[d] Daily exposure compared with 0.4 mg/day exposure from the consumption of 2 l water containing 0.2 mg/l.

equivalent of a lifetime, these rats showed no overt signs of cyanide poisoning, and hematological values were normal. Gross and microscopic examinations of tissues revealed no abnormalities. The only abnormality found was an elevation of thiocyanate levels in the liver and kidneys. Consequently, the ADI for man is derived by taking the no-observable-adverse-effect level in mammals (12 mg/kg/day) multiplied by the weight of the average man (70 kg) and dividing by a safety factor of 100. This safety factor was derived by methods discussed in the Federal Register (44 FR 15980). Thus,

ADI = 12 mg/kg/day x 70 kg ÷ 100 = 8.4 mg/day.

The equation for calculating the criterion for the cyanide content of water given an Acceptable Daily Intake is

$$2X + [(0.0065)(F)(X)] = ADI$$

Where

2 = amount of drinking water, l/day

X = cyanide concentration in water, mg/l

0.0065 = amount of fish consumed, kg/day

F = bioconcentration factor, mg cyanide/kg fish per mg cyanide/l water

ADI = limit on daily exposure for a 70 kg person = 8.4 mg/day

$$2X + (0.0065)(1)X = 8.4$$

$$X = 4.19 \text{ mg/l (or } \approx 4.2 \text{ mg/l)}$$

Thus, the current and recommended criterion (0.2 mg/l) has a margin of safety of 21.0 (4.2 ÷ 0.2).

No new additional evidence was encountered to suggest that the 1962 PHS Drinking Water Standard for cyanide should be lowered. The concentration of 0.2 mg/l or less is easily achieved by proper treatment and concentrations in excess of that amount have been

encountered only on rare occasions in U.S. water supplies. The experience since 1962 suggests that 0.2 mg CN^-/l is a safe criterion for man.

Although a case could be made for using the epidemiologic data (El Ghawari, et al. 1975) or the rat feeding study (Howard and Hanzal, 1955) to derive alternative higher criteria, such an approach is not recommended at this time. The epidemiologic data was obtained on a very limited number of individuals exposed by inhalation rather than oral administration, on which there was a statistically significant biological effect. In the rat feeding study, cyanide was added to the chow by fumigation. Consequently, some uncertainty exists concerning the actual dose levels. The current PHS drinking water standard represents a body of human experience which has proven both protective and achievable. At this time, the epidemiologic data and animal toxicity studies are not of sufficiently high quality to justify a water quality criterion above the PHS standard.

REFERENCES

American Cyanamid Co. 1959. Report on sodium cyanide: 30-Day repeated feedings to dogs. Central Med. Dept.

Braico, K.T., et al. 1979. Laetrile intoxication: Report of a fatal case. New England Jour. Med. 300: 238.

Brink, N.G., et al. 1950. Vitamin B_{12}: The identification of vitamin B_{12} as a cyano-cobalt coordination complex. Science. 112: 354.

Brobeck, T.R. 1973. Best and Taylor's Physiological Basis of Medical Practice. 9th ed. Williams and Wilkins Co., Baltimore.

Chen, K.K. and C.L. Rose. 1952. Nitrite and thiosulfate therapy in cyanide poisoning. Jour. Am. Med. Assoc. 149: 113.

Conchie, J., et al. 1959. Mammalian glycosidases distribution in the body. Biochem. Jour. 71: 318.

Davison, V. 1969. Cyanide poisoning. Occup. Health. 21: 306.

de Duve, C., et al. 1955. Tissue fractionation studies: 6. Intracellular distribution patterns of enzymes in rat-liver tissue. Biochem. Jour. 60: 604.

Drinker, P. 1932. Hydrocyanic acid gas poisoning by absorption through the skin. Jour. Ind. Hyg. 14: 1.

Dudley, H.C., et al. 1942. Toxicology of acrylonitrile (vinyl cyanide): II. Studies of effects of daily inhalation. Jour. Ind. Hyg. Toxicol. 24: 255.

El Ghawabi, S.H., et al. 1975. Chronic cyanide exposure: a clinical, radioisotope, and laboratory study. Br. Jour. Ind. Med. 32: 215.

Fassett, D.W. 1963. Cyanides and Nitriles. In: D.W. Fassett and D.D. Irish, (eds.) Industrial Hygiene and Toxicology. 2nd ed. John Wiley and Sons, Inc., New York. 2: 1991.

Friedberg, K.D. and H.A. Schwarzkopf. 1969. Blausaureexhalation bei der Cyanidvergiftung (The exhalation of hydrocyanic acid in cyanide poisoning). Arch. Toxicol. 24: 235.

Gettler, A.O. and A.V. St. George. 1934. Cyanide poisoning. Jour. Clin. Pathol. 4: 429.

Gosselin, R.E., et al. 1976. Clincial Toxicology of Commerical Products. 4th ed. Williams and Wilkins Co., Baltimore, Maryland.

Hayes, W.T., Jr. 1967. The 90-dose LD_{50} and a chronicity factor as measures of toxicity. Toxicol. Appl. Pharmacol. 11: 327.

Health and Welfare, Canada. 1977. Cyanide-drinking water criteria review. Document furnished by Dr. Peter Toft.

Hertting, G., et al. 1960. Untersuchungen uber die Folgen einer chronischen Verabreichung akut toxicher Dosen von Natriumcyanid an Hunden. Acta. Pharmacol. Toxicol. 17: 27.

Heymans, C. and E. Neil. 1958. Cardiovascular Reflexes of Chemoreceptor Origin. In: Reflexogenic Areas of the Cardiovascular System. J.A. Churchill, Ltd., London. p. 176.

Himwich, W.A. and J.P. Saunders. 1948. Enzymatic conversion of cyanide to thiocyanate. Am. Jour. Physiol. 153: 348.

Howard, J.W. and R.F. Hanzal. 1955. Chronic toxicity for rats of food treated with hydrogen cyanide. Jour. Agric. Food Chem. 3: 325.

Hrizu, D., et al. 1973. Cytostatic effects of potassium sulfocyanate in vivo and in vitro. Arch. Roum. Pathol. Exp. Microbiol. 32: 155.

Johnstone, R.A.W. and J.R. Plimmer. 1959. The chemical constitutents of tobacco and tobacco smoke. Chem. Rev. 59: 885.

Kirk, R.L. and N.S. Stenhouse. 1953. Ability to smell solutions of potassium cyanide. Nature. 171: 698.

Knowles, E.L. and J.T.B. Bain. 1968. Medical cover required in large scale production of cyanides and hydrocyanic acid. Chem. Ind. 8: 232.

Lawes, B.C. 1972. Control of cyanides in plating shop effluents: What's on the shelf now? Plating. 59: 394.

Leduc, G., et al. 1973. Use of sodium cyanide as a fish eradicant in some Quebec lakes. Natur. Can. 100: 1.

Lehninger, A.L. 1975. Biochemistry. 2nd ed. Worth Publishers, Inc., New York.

Lendle, L. 1964. Werkungsbedungungen von blausaure und schwefelwasserstoff und moglichreiten der vergiftungsbehandlung. Jap. Jour. Pharmacol. 14: 215.

McCabe, L.J., et al. 1970. Survey of community water supply systems. Jour. Am. Water Works Assoc. 62: 670.

McNerney, J.M. and H.H. Schrenk. 1960. The acute toxicity of cyanogen. Am. Ind. Hyg. Assoc. Jour. 21: 121.

Miller, L.P. 1973. Glycosides. In: Phytochemistry. Vol. I. Van Nostrand Reinhold Co., New York. p. 297.

National Institute for Occupational Safety and Health. 1976. Criteria for recommended standard...Occupational exposure to hydrogen cyanide and cyanide salts (NaCN, KCN and $Ca(CN)_2$). NIOSH Publ. No. 77-108. Dep. Health Edu. Welfare. U.S. Gov. Printing Off., Washington, D.C.

Nicholls, P. 1975. The effect of sulfide on cytochrome aa_3. Isosteric and allosteric shifts of the reduced peak. Biochem. Biophys. Acta. 396: 24.

Nowinski, W.W. and J. Pandra. 1946. Influence of sodium thiocyanate on the development of the chick embryo. Nature. 157: 414.

Ortolani, G. 1969. The action of sodium thiocyanate (NaSCN) on the embryonic development of the ascidians. Acta Embryol. Exp. 27-34.

Osuntokun, B.O. 1968. An ataxic neuropathy in Nigeria. Brain. 91: 215.

Ottinger, R.S., et al. 1973. Recommended methods for reduction, neutralization, recovery, or disposal of hazardous waste. Vol 1. EPA-670/2-73-053-a, U.S. EPA, Washington, D.C.

Perry, I.H. 1935. The effect of prolonged cyanide treatment on body and tumor growth in rats. Am. Jour. Cancer. 25: 592.

rettigrew, A.R. and G.S. Fell. 1973. Microdiffusion method for estimation of cyanide in whole blood and its application to the study of conversion of cyanide to thiocyanate. Clin. Chem. 19: 466.

Potter, A.L. 1950. The successful treatment of two recent cases of cyanide poisoning. Br. Jour. Ind. Med. 7: 125.

Prentiss, A.M. 1937. Systemic Toxic Agents. In: Chemicals in War. McGraw-Hill Book Co., Inc., New York. p. 170.

Reed, A.K., et al. 1971. An investigation of techniques for removal of cyanide from electroplating wastes. Rep. No. 12010 EIE 11/71. U.S. Gov. Printing Off., Washington, D.C.

Rosehart, R.G. and R. Chu. 1974. Cyanide destruction in mine wastewater. Water Pollut. Res. Can. 85.

Smith, L., et al. 1977. The effect of methemoglobin on the inhibition of cytochrome c oxidase by cyanide, sulfide or azide. Biochem. Pharmacol. 26: 2247.

Smith, R.P. and R.E. Gosselin. 1979. Hydrogen sulfide poisoning. Jour. Occup. Med. 21: 93.

Smith, R.P. and M.V. Olson. 1973. Drug-induced methemoglobinemia. Semin. Hematol. 10: 253.

Sorbo, B.H. 1953. On the substrate specificity of rhodanese. Acta Chem. Scand. 7: 32.

Stephan, C.E. 1980. Memorandum to J. Stara. U.S. EPA. May 5.

Terrill, J.B., et al. 1978. Toxic gases from fires. Science. 200: 1343.

The Oak Ridger. 1975. State says cyanide caused lake fishkill. Oak Ridge, Tennessee. September 5.

Tovo, S. 1955. Poisoning due to KCM absorbed through skin. Mineria Med. 75: 158.

Towill, L.E., et al. 1978. Reviews of the environmental effects of pollutants: V. Cyanide. U.S. EPA. NTIS-PB 289-920.

U.S. Public Health Service. 1962. Drinking water standards. PHS Publ. No. 956. U.S. Gov. Printing Off., Washington, D.C.

Walton, D.C. and M.G. Witherspoon. 1926. Skin absorption of certain gases. Jour. Pharmacol. Exp. Ther. 26: 315.

Watson, M.R. 1973. Cyanide Removal from Water. In: Pollution Control in Metal Finishing. Noyes Data Corp., Park Ridge, New Jersey. p. 147.

Way, J.L., et al. 1966. Effect of oxygen in cyanide intoxication: I. Prophylactic protection. Jour. Pharmacol. Exp. Ther. 153: 331.

Williams, R.T. 1959. Detoxication Mechanisms. 2nd ed. John Wiley and Sons, Inc., New York.

Wilson, J. and D.M. Matthews. 1966. Metabolic interrelationships between cyanide, thiocyanate, and vitamin B_{12} in smokers and non-smokers. Clin. Sci. 31: 1.

Wolfsie, J.H. and C.B. Shaffer. 1959. Hydrogen cyanide. Jour. Occup. Med. 1: 281.

Wood, J.L. and S.L. Cooley. 1956. Detoxication of cyanide by cystine. Jour. Biol. Chem. 218: 449.